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Fulbright & Jaworski LLP
600 Congress Avenue
Suite 2400
Austin, TX 78701

EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/669,301	Applicant(s) KUDLICKI ET AL.	
	Examiner Arun Chakrabarti	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-16,18,20,23,44 and 46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-16,18,20,23,44 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Specification

1. Claims 8, 17, and 22 have been canceled without prejudice towards further prosecution. Claims 1-7, 9-16, 18, 20, 23, 44, and 46 have been amended. New claims 51-55 have been amended.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-5, 7, 9, 10, 12, 13, 15, 16, 18, 20, and 23 are rejected under 35 U.S.C. 103(a) over Lee et al. (Immunochemistry, (1972), Vol. 9, pages 210-213) in view of Cazenave (Proceedings of the National Academy of Sciences (USA), (1977), Vol. 74 (11), pages 5122-5125).

Lee et al teach a method comprising:

a) obtaining at least a first nuclease inhibitor (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, line 4, Magnesium Chloride in this case);

b) obtaining at least a second nuclease inhibitor (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 4-5, heparin in this case); and

c) obtaining a composition (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 1-5, rabbit spleen tissue in phosphate buffered saline in this case); and

d) admixing the nuclease inhibitors and the composition (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 1-10).

Lee et al teach the method, wherein admixing is carried out by mixing the first and second nuclease inhibitors to form a nuclease inhibitor cocktail and mixing the nuclease inhibitor cocktail with the composition (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 1-10).

Lee et al teach the method, wherein obtaining the first and second nuclease inhibitors comprises obtaining a nuclease inhibitor cocktail comprising the first and second nuclease inhibitor (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 4-5, Magnesium Chloride and heparin in this case).

Lee et al inherently teach the method, wherein the composition comprises at least one nuclease and RNA (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 1-10). This inherence is deduced from the fact that a freshly excised rabbit spleen naturally contains several nuclease and RNA.

Lee et al inherently teach the method, wherein the composition is a reagent used in molecular biology (MATERIALS AND METHODS Section, and RESULTS AND DISCUSSION Section). This inherence is deduced from the fact that polyribosomes (site of protein synthesis in cells) isolation is essentially under the domain of molecular biology.

Lee et al teach the method, wherein the second nuclease inhibitor is heparin (Page 211, MATERIALS AND METHODS Section, Isolation of polysome fractions Subsection, lines 4-5,)

Lee et al teach the method, further defined as a method of inhibiting nucleases in the composition (Page 211, lines 2-3 and MATERIALS AND METHODS Section, and RESULTS AND DISCUSSION Section).

Lee et al teach the method, wherein the second nuclease inhibitor is a polyclonal anti-ribonuclease antibody and capable of binding to mRNA ribonuclease (Figure 1 and

MATERIALS AND METHODS Section, second paragraph, and Introduction, Second paragraph, first five lines) and the first nuclease inhibitor is Magnesium chloride .

Lee et al do not teach the method, wherein the anti-ribonuclease antibody is an anti-RNAse 1 antibody.

Cazenave teaches the method, wherein the anti-ribonuclease antibody is an anti-RNAse 1 antibody (Abstract).

Lee et al do not teach the method, wherein the anti-ribonuclease antibody is an anti-RNAse T1 antibody and anti-deoxyribonuclease antibody.

Lee et al suggest the method, wherein the anti-ribonuclease antibody is against all other nuclease present in the crude tissue (Page 212, last sentence to page 213, line 1).

Lee et al do not teach the method, wherein the anti-ribonuclease antibody is capable of binding to micrococcal nuclease.

Cazenave teaches the method, wherein the anti-ribonuclease antibody is capable of binding to micrococcal nuclease (Page 5124, Column 1, second paragraph).

Lee et al do not teach the method, wherein the second and third nuclease inhibitor are anti-ribonuclease antibody.

Cazenave teaches the method, wherein the equivalent second and third nuclease inhibitor are anti-ribonuclease antibody. (Abstract and MATERIALS AND METHODS Section).

Lee et al do not teach the method, wherein the first nuclease inhibitor is an anti-nuclease antibody.

It would have been prima facie obvious to an ordinary practitioner to switch the order of selecting the inhibitors of nuclease as MPEP 2144.04 further states, " *In re Gibson,* 39 F.2d 975, 5 USPQ 230 (CCPA 1930) Selection of any order of mixing ingredients is *prima facie* obvious".

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine, within the method of inhibiting the nuclease of Lee et al., mixtures of anti-RNAse 1 antibodies of Cazenave since Lee et al state, "On the basis of this explanation, it may be suggested that the procedure for isolation of polysomes could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract (Page 212, last sentence to page 213, line 1)". By employing scientific reasoning, an ordinary artisan would have been motivated by the express statement of Lee et al to substitute and combine, within the method of inhibiting the nuclease of Lee et al., mixtures of anti-RNAse 1 antibodies of Cazenave in order to achieve the express advantages, as noted by Lee et al. , of a strategy which provides the procedure for isolation of polysomes that could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract.

4. Claims 1-5, 7, 9, 10-16, 18-20, and 23 are rejected under 35 U.S.C. 103(a) over Lee et al. (Immunochemistry, (1972), Vol. 9, pages 210-213) in view of Cazenave (Proceedings of the National Academy of Sciences (USA), (1977), Vol. 74 (11), pages 5122-5125) further in view of Bucala et al. (U.S. Patent 6,110,968) (August 29, 2000).

Lee et al in view of Cazenave teach method of claims 1-5, 7, 9, 10, 12, 13, 15, 16, 18, 20, and 23 as described above.

Lee et al in view of Cazenave do not teach the method, wherein the anti-ribonuclease antibody is an anti-RNAse A antibody.

Bucala et al. teach the method, wherein the anti-ribonuclease antibody is an anti-RNAse A antibody (Column 11, lines 14-18).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine, within the method of inhibiting the nuclease of Lee et al. in view of Cazenave, an anti-RNAse A antibody of Bucala et al. since Bucala et al state, "To assess the formation of dimers, the samples were subjected to SDS-PAGE under reducing conditions, followed by transfer to cellulose and western blotting with a rabbit anti-RNAse A antibody (Column 11, lines 14-17)". Moreover Lee et al provides further motivation as Lee et al state, "On the basis of this explanation, it may be suggested that the procedure for isolation of polysomes could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract (Page 212, last sentence to page 213, line 1)". By employing scientific reasoning, an ordinary artisan would have been motivated by the express statement of Bucala et al to substitute and combine, within the method of inhibiting the nuclease of Lee et al. in view of Cazenave, an anti-RNAse A antibody of Bucala et al. in order to achieve the express advantages, as noted by Bucala et al. , of a method which provides the assessment of the formation of dimers

between antigen and antibody and also to achieve the express advantages, as noted by Lee et al. , of a strategy which provides the procedure for isolation of polysomes that could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract.

5. Claims 1-7, 9, 10, 12, 13, 15, 16, 18, 20, 21, 23, 37-49, and 51-55 are rejected under 35 U.S.C. 103(a) over Lee et al. (Immunochemistry, (1972), Vol. 9, pages 210-213) in view of Cazenave (Proceedings of the National Academy of Sciences (USA), (1977), Vol. 74 (11), pages 5122-5125) further in view of Murphy et al. (BioTechnique, (1995), Vol. 18(6), pages 1069-1073).

Lee et al in view of Cazenave teach method of claims 1-5, 7, 9, 10, 12, 13, 15, 16, 18, 20, and 23 as described above.

Lee et al in view of Cazenave do not teach the method, wherein the composition is further defined as a transcription/translation reaction comprising both DNA and RNA.

Murphy et al. teach the method, wherein the composition is further defined as a transcription/translation reaction comprising both DNA and RNA.. (Abstract and MATERIALS AND METHODS Section, In vitro transcription and translation Subsection and cDNA synthesis Subsection, Page 1069).

Lee et al in view of Cazenave do not teach the method, wherein the nuclease inhibitor is human placental ribonuclease inhibitor.

Murphy et al. teach the method, wherein the nuclease inhibitor is human placental ribonuclease inhibitor (Introduction Section, Column 1, last sentence).

Lee et al in view of Cazenave do not teach the method, wherein the anti-ribonuclease antibody is capable of binding to S1 nuclease and anti-deoxyribonuclease antibody.

Lee et al suggest the method, wherein the anti-ribonuclease antibody is against all other nuclease present in the crude tissue (Page 212, last sentence to page 213, line 1).

Lee et al in view of Cazenave do not teach the method, wherein the nuclease inhibitor cocktail and a lysate are placed in the in vitro translation reaction.

Murphy et al. teach the method, wherein the nuclease inhibitor cocktail and a lysate are placed in the in vitro translation reaction. (Abstract and MATERIALS AND METHODS Section, In vitro transcription and translation Subsection, Page 1069).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine, within the method of inhibiting the nuclease of Lee et al. in view of Cazenave, the nuclease inhibitor cocktail and a lysate placed in the in vitro translation reaction. of Murphy et al. since Murphy et al state, "It has a high specific activity, enhanced temperature stability, broad reaction pH range and significantly greater cost-effectiveness than commercial HPRI. Prime inhibitor is suitable for use in in vitro transcription, in vitro translation, first and second-strand cDNA synthesis, preparation of RNA and mRNA, and reverse transcription polymerase chain reaction (Abstract, last two sentences)". Moreover, Lee et al state, "On the basis of this explanation, it may be suggested that the procedure for isolation of

polysomes could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract (Page 212, last sentence to page 213, line 1)". By employing scientific reasoning, an ordinary artisan would have been motivated by the express statement of Murphy et al to substitute and combine, within the method of inhibiting the nuclease of Lee et al. in view of Cazenave, the nuclease inhibitor cocktail and a lysate placed in the in vitro translation reaction. of Murphy et al. in order to achieve the express advantages, as noted by Murphy et al. , of inhibitors which has a high specific activity, enhanced temperature stability, broad reaction pH range and significantly greater cost-effectiveness than commercial HPRI and which is suitable for use in in vitro transcription, in vitro translation, first and second-strand cDNA synthesis, preparation of RNA and mRNA, and reverse transcription polymerase chain reaction, and also in order to achieve the express advantages, as noted by Lee et al. , of a strategy which provides the procedure for isolation of polysomes that could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract.

Response to Amendment

6. In response to amendment, all 112 (second paragraph) rejection and 102 (b) rejections are hereby withdrawn. However, new 103(a) rejections based on the same prior arts are hereby included.

Response to Arguments

7. Applicant's arguments filed on February 26, 2002 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Lee et al since Lee et al state, "On the basis of this explanation, it may be suggested that the procedure for isolation of polysomes could be further improved by the use of polyspecific immunosorbents prepared with antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract (Page 212, last sentence to page 213, line 1)". Therefore, any numbers and combinations of antibodies elicited against r-s-RNase and all other nucleases present in the crude tissue extract can be used in order to further improve the isolation of polysomes as well as extraction of nucleic acids from any mixtures wherein nucleases may be present.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

March 13, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600